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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
WHALEY, PABLO S	
ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/724,910	PASIKA ET AL.	
	Examiner	Art Unit	
	PABLO WHALEY	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *52-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims Under Examination

Claims 52-57 are pending. Claims 1-51 are cancelled.

Priority

This application has been granted the benefit of priority to US Provisional Application 60/227,556, filed 8/23/2000.

Specification

The amended specification, filed 06/13/2008, which deletes subject matter directed to signals is acknowledged.

Claim Objections

The objection to claims 52 and 55 for being grammatically incorrect with withdrawn in view of applicant's amendment filed 06/13/2008.

Withdrawn Rejections

The rejection of claims 52-57 under 35 U.S.C. 112, second paragraph, is withdrawn in view of applicant's arguments filed 06/13/2008.

Claim Rejections - 35 USC §101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

This rejection is newly applied in view of recent court decisions.

Claims 52- 57 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter. Claims 52-57 are non-statutory because they read on abstract ideas. The prohibition on patenting abstract ideas has two distinct aspects: (1) when an abstract concept has no claimed practical application, it is not patentable; (2) while an abstract concept may have a practical application, a claim reciting an algorithm or abstract idea can state statutory subject matter only if it is embodied in, operates on, transforms, or otherwise is tied to another class of statutory subject matter under 35 U.S.C. §101 (i.e. a machine, manufacture, or composition of matter). (See In re Comiskey, Fed. Cir., No. 2006-1286, 9/20/07; Gottschalk v. Benson, 409 U.S. 63, 175 USPQ 673, 1972).

In the instant case, claims 52-53 do not qualify as a statutory process because the method steps that are critical to the invention are "not limited to a particular apparatus or machine." To qualify as a statutory process, the critical method steps recited in claims 52-53 should positively recite the other statutory class (the thing or product) to which it is tied, for example by identifying the apparatus that accomplishes the method steps, or positively recite the subject mater that is being transformed, for example by identifying the material that is being changed to a different state or thing. Nominal data gathering or post solution activity steps in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. Preamble limitations that require the claimed process to comprise machine implemented steps will not be

considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. The applicants are cautioned against introduction of new matter in an amendment.

In addition, claims 54-57 are drawn to computer readable medium containing instructions for carrying out a processes. The specification does not limit the claimed computer readable medium to physical medium or machine. Therefore claims 54-57 do not qualify as a statutory process because the method steps that are critical to the invention are "not limited to a particular apparatus or machine." To qualify as a statutory process, the critical method steps recited in claims 54-57 should positively recite the other statutory class (the thing or product) to which it is tied, for example by identifying the apparatus that accomplishes the method steps, or positively recite the subject mater that is being transformed, for example by identifying the material that is being changed to a different state or thing. Nominal data gathering or post solution activity steps in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. Preamble limitations that require the claimed process to comprise machine implemented steps will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. The applicants are cautioned against introduction of new matter in an amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 52-57 are rejected under 35 U.S.C. 103(a) as being made obvious by Ng (School of Computer Science, 1998, Abstract and p. 1-389), in view of Gilchrist et al. (US 5,916,747; Issued Jun. 29, 1999), and in view of Kaiser et al. (International Conference on Acoustics, Speech, and Signal Processing, 1990, Vol. 1, p.381-384).

Ng teaches a novel computer-based analysis method (FAST-MAP) for fully automated genotyping that accurately preprocesses and calls alleles from DNA fragment data [Abstract]. Ng shows receiving fragment analysis data representing intensity values and nucleic acid fragment length information [p.97-102, Section 5.3.3]. Ng shows plotting a profile of the original electropherogram signal [p.98, Fig. 5.10]. Ng shows additionally fitting local maximum and local minimum values in the signal data, and dividing the signal data into panels at local maxima [p.97, Section 5.3.3, p.98, Fig. 5.9, p.98, Fig. 5.10, p.102, Fig. 5.15], which shows forming a signal envelope and dividing a signal envelope. It is noted that the specification [p.14, ¶1] does not provide a limiting definition for "signal envelope." Ng teaches binning and quantitation for each marker band's relative DNA concentration defined by the area under the peak in the intensity profile using least squares calculations [p.84, ¶1, p.93, Step 5 and Section 5.3, p.96, Box 5.3, step 1]. Ng shows determining local maximum and local minimum values in the enveloped data and dividing the signal data into panels at each local maximum [p.98, Fig. 5.9, p.102, Fig.

5.15]. Ng also provides for "outputting" allele calls [p.279]. Ng shows algorithms (i.e. tests) for enumerating over candidate alleles based on ratios, and locally searching for best amplification ratios in a specified range (i.e. window) based on a "sum of squares" error calculation [p.142, Box 6.8]. Ng teaches an ENUM algorithm that detects three candidate alleles and ranks all possible combinations (i.e. first, second, and third test) and reports the top three candidates [p.144, ¶ 2]. Ng uses "binned" data obtained from signal peaks with the maximum intensity to obtain candidate alleles [p.143, Fig. 6.12, Top and Middle Windows, p.145, Fig. 6. 13], which shows the use of panels with the greatest energy corresponding to "maximum intensity" values.

Ng does not specifically teach dividing the signal envelope into panels with boundaries at each local minimum, as in claims 52 and 55.

Ng does not specifically teach computing an energy value for each panel, as in claims 52, 53, 55, and 56.

Gilchrist et al. teaches a method for alignment and normalization of trace data signals for improved base calling. In particular, data that includes creating windows from trace data, determining the peaks of the analysis data, and determining peaks and values (i.e. maxima and minima) [Fig. 4A and 4B] and [Col. 6, lines 40-60]. In particular, the windows occur at peak minima. Gilchrist also show applying algorithms to each point of trace data within a window to modify its position and change the cost area function (i.e. energy). The presentation of aligned data sets is then made available for further use for base-calling and other purposes [Col. 8, lines 58-67]. Gilchrist also show a preferred approach to base-calling of aligned data wherein minimum peak height is selected by the user to avoid spurious results [Col. 9, lines 1-10].

Kaiser teaches standard methods for calculating the energy of any signal [Abstract, Introduction]. In particular, Kaiser teaches that energy calculations are commonly determined by the sum of squares

[Introduction] and shows energy calculations for signals with multiple components [p.384, Col. 1], as in claims 52, 53, 55, and 56.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of Ng by calculating energy value for each panel, since Kaiser teaches a well known and predictable method for determining the energy of a signal. In addition, Ng determines the area under each peak within the intensity profile curves using least squares calculations [p.84, ¶1, p.93, Step 5 and Section 5.3], which suggests energy calculations in view of the instant specification [p.14], which shows that energy values are calculated by summing the square of each element in the panel. One of ordinary skill in the art would be motivated to make the above modification in order use well known energy calculation methods for signal analysis.

It would further have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of Ng et al. by dividing the signal into panels at local minimum values, as taught by Gilchrist, since Ng teaches the alignment of marker band data [p. 91 and p.118], resulting in the practice of the instantly claimed invention with predictable results. One of ordinary skill in the art would be motivated to make the above modification in order to exclude local minimum values from the computational process, as suggested by Ng [p.104, ¶3] and to provide an improved method of base-calling, as suggested by Gilchrist [Col. 2, lines 5-25].

Claims 52-57 are rejected under 35 U.S.C. 103(a) as being made obvious by Northeastern University (WO/1999/53423; International Publication Date: Oct. 21, 1999), in view of ABI PRISM Genotyper 2.5 User's Manual (PE Biosystems, Copyright 1998, p.1-354).

Northeastern teaches a base-calling algorithm. Northeastern teaches determining peaks of fragment analysis data representing intensity values [page 1 (Background) and Figure 2B]. Northeastern teaches a method for forming a signal envelop using maximum signals of trace data [p.32, last ¶ through p.33, ¶1] and methods for outlining the data [p.15] based on least-square fitting of spectral data. Northeastern detecting peaks based on thresholding or local maxima/minima; and assigning base calls if a plurality of rules are met [p.13 and p.19-23]. A peak subdivision procedure for dividing peak data based local minima [p.37-38] is shown. Northeastern shows dividing signal data into regions based on local minima values when local maxima peaks are separated by large valleys [p.29, lines 10-20], which equates to dividing a signal into panels at each local minima. The greatest integrated signal in each peak-containing region is determined [p.30], which equates to determining energy values for each panel. Locations for all local minima are determined for peak containing windows based on second derivatives functions that include peak width [p.31]. Allele calls are reported to a user [Fig. 4] and [p.15, ¶1].

Northeastern does not specifically teach computer a first and second ratio of energy values, as in claims 52, 54, 55, and 57.

ABI PRISM teaches a genotyping software system providing for manual and automated labeling and analysis of DNA fragments. ABI PRISM generally teaches receiving fragment analysis data [p.71, Section 3-13]; displaying and providing user with means to label signals comprising peak and size information [p.116]; user-definable categories for defining specific peak ranges, peak maxima and minima [p.119-120], and specifically teaches methods for comparing data quality of any peaks based on "ratios" and "sum of squares" [p.210 and p.212].

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify the method of Northeastern to calculate first and second ratios of energy values as taught by ABI PRISM, since ABI PRISM suggests linking their software to third-party programs or files for further analysis of fragment peak data [p.278, Section 11-1, p. 292, Section 12-7]. One of ordinary

skill in the art would have been motivated to combine the above teachings in order to improve base-calling accuracy using automated quality control techniques, as suggested by ABI PRISM [p.210 and p.212].

Response to Arguments

Applicant's arguments, filed 06/13/2008, that Ng does not teach computing an energy value for each panel have been fully considered and are persuasive. However, applicant's arguments are moot in view of the new grounds of rejection.

Applicant's additional arguments, filed 06/13/2008, regarding the rejection of claims 52-57 under 35 U.S.C. 103(a) as being made obvious by Ng in view of Gilchrist have been fully considered but are not persuasive for the following reasons.

In response to applicant's argument that Ng does not teach forming a signal envelope, Ng shows a search algorithm for graphically determining local maximum and local minimum values in the fitted data and dividing the signal data into panels at local maxima [p.97, Section 5.3.3, p.98, Fig. 5.9, p.98, Fig. 5.10, p.102, Fig. 5.15]. The specification [p.14, ¶1] does not provide a limiting definition, despite applicant's assertion to the contrary. Therefore, Ng shows forming a signal envelope from peaks.

In response to applicant's argument that it is impossible for Gilchrist to teach dividing an envelope signal at each local minima, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See In re Keller, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Ng teaches dividing an enveloped signal at local maxima. Gilchrist teaches creating windows from trace data, and determining peaks and valleys in the data (i.e. maxima and minima) [Fig. 4A and 4B, Col. 6, lines 40-60]. Gilchrist also show a preferred approach to base-calling of aligned data wherein minimum

peak height is selected by the user to avoid spurious results [Col. 9, lines 1-10]. Therefore, it would have been obvious to one of ordinary skill in the art to determining local minima values in signal data, since Ng already shows methods for identifying local maxima in the data and signal Gilchrist shows evaluating trace data at local maxima and local minima. The rationale would have been to identify least favorable data sets for exclusion. For these reasons, this rejection is maintained.

Applicant's arguments, filed 06/13/2008, regarding the rejection of claims 52-57 under 35 U.S.C. 103(a) as being made obvious by Northeastern University in view of ABI PRISM have been fully considered but are not persuasive for the following reasons.

In response to applicant's argument that Northeastern does not teach determining peaks of fragment analysis, see Northeastern page 1 (Background) and Figure 2B.

In response to applicant's argument that Northeastern does not teach forming a signal envelop, Northeastern shows enveloping of maximum signals from trace data [p.32, last ¶ through p.33, ¶1] and methods for outlining the data [p.15] based on least-square fitting of spectral data.

In response to applicant's argument that Northeastern does not teach dividing the signal into panels, or computing an energy value for each panel, Northeastern shows dividing the signal into regions based on local minima and maxima [p.29, lines 10-20] and determining the greatest integrated signal in each peak-containing region [p.30], which equates to determining energy values for each panel.

In response to applicant's arguments that the concepts of a signal envelope and computation of energy in a panel are absent, Northeastern shows determining integrated area under signals for each peak-containing region [p.30 and p.33]. It is well known that mathematical methods for determining an area under a curve can be determined by the integration of values under that curve using a sum of squares. Furthermore, the specification [p.14] shows that energy values are calculated by summing the square of

each element in the panel. Therefore, Northeastern shows methods for computing energy values based on summing of signals under curves.

In response to applicant' arguments that Northeastern does not teach computing first and second ratios of the energy values, ABI PRISM teaches methods for comparing data quality of any peaks based on "ratios" and "sum of squares" calculations [p.210 and p.212], which makes obvious the determining of first and second ratio values based on sum of square calculations. The rationale would have been to compare multiple ratio values for purposes of quality control. For these reasons, this rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Pablo Whaley whose telephone number is (571)272-4425. The examiner can normally be reached on 9:30am - 6pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached at 571-272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Pablo S. Whaley/

Patent Examiner

Art Unit 1631

/John S. Brusca/

Primary Examiner, Art Unit 1631